

# Beryllium BioBank

To Promote Future Research on the Effects of Beryllium Exposure

**Lisa A. Maier, MD, MSPH**

**Professor, National Jewish Health**

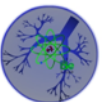
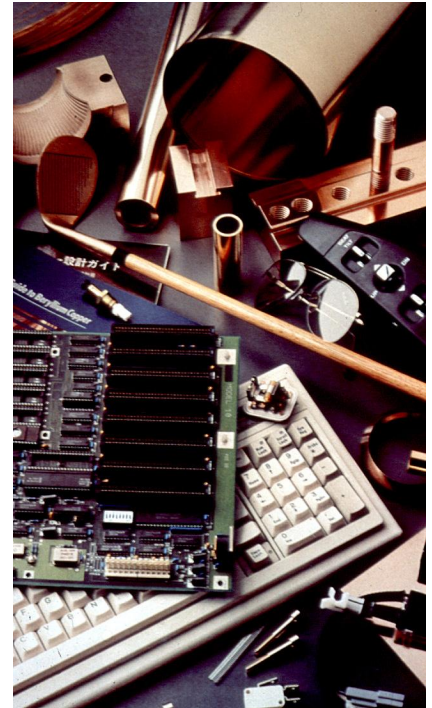
**MaierL@NJHealth.org**

October 2012



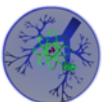
# *Goal of the Department of Energy Beryllium BioBank*

- To facilitate future beryllium disease research and improve our understanding of beryllium-related health effects*
- by collecting and archiving biological specimens and associated clinical data from patients with chronic beryllium disease, beryllium sensitization, and those exposed to beryllium who are non-sensitized.*



# Specifically: A resource to potentially...

- Identify exposure and genetic risk factors associated with BeS and CBD
- Improve the detection of BeS and CBD
- Define new therapeutics to be tested in the treatment of CBD
- Understand the immune and inflammatory mechanisms of CBD
- Develop new biological markers of exposure, biological effect and disease
- Define clinical and physiologic phenotypes of CBD



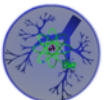
# Repository Roles

US  
Department  
of Energy  
(DOE)

- Oversight and funding

Steering  
Committee

- DOE Project Officer
- Steering Committee Chair
- PI's- Clinical Centers, DCC, Core Laboratories
- Former Workers



# Centers

**Lead Clinical Center**  
**National Jewish Health**  
(Lisa Maier, MD, MSPH)



- Recruit, consent and retain participants      —————>      ▪ Collect clinical data
- Transmit data electronically to the DCC
- Ship specimens and CT/CXR scans to the Core Laboratories and DCC

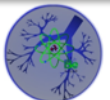


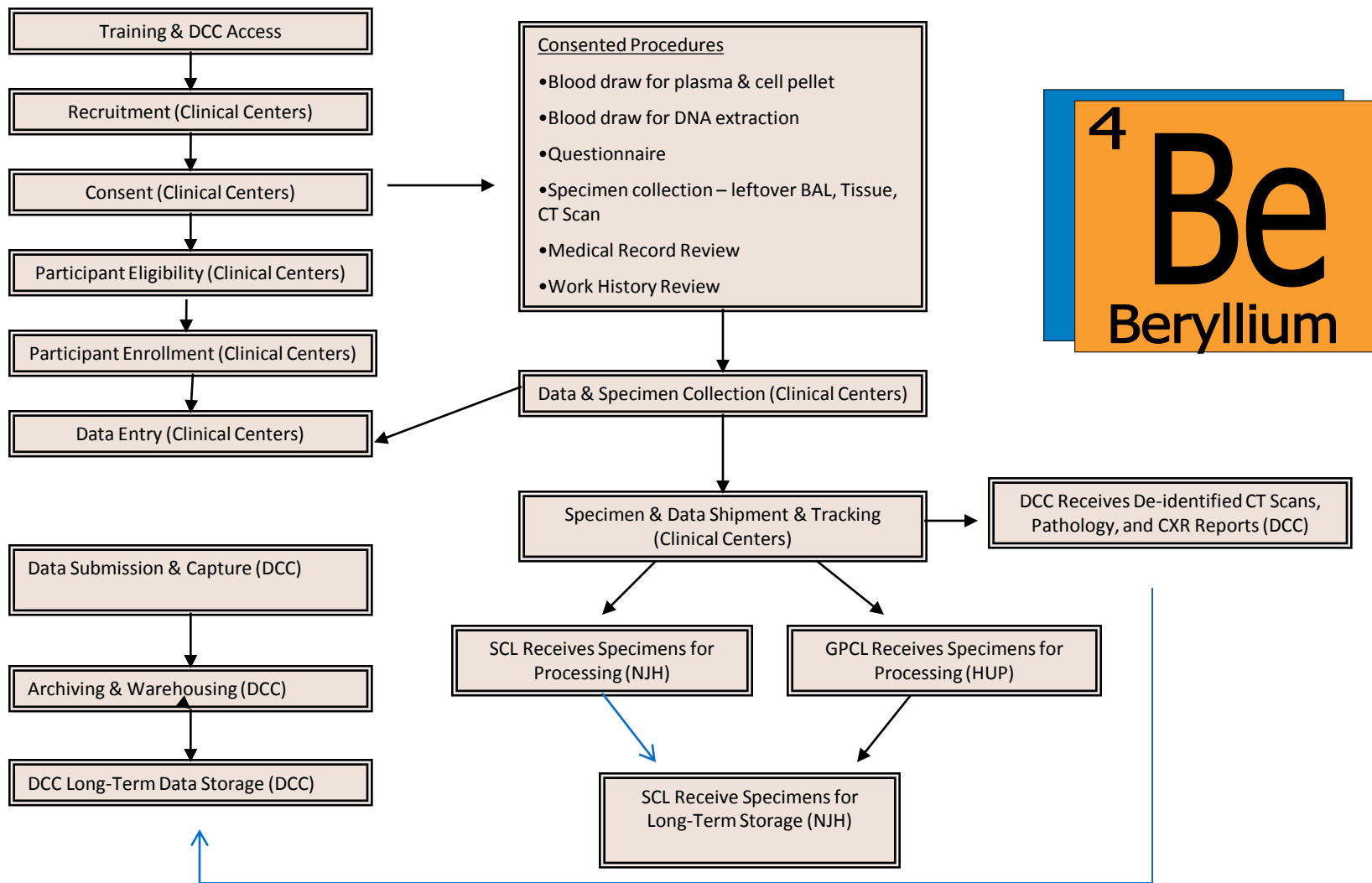
**University of Pennsylvania**  
(Milt Rossman, MD)  
**University of California, San Francisco**  
(John Balmes, MD)  
**University of California, Los Angeles**  
(Philip Harber, MD)  
**East Tennessee Pulmonary Associates**  
**Oak Ridge Associated Universities**  
(Donna Cragle, PhD)



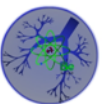
**Data Coordinating Center, University of Colorado, CSH**  
**Lee Newman, MD, MA**

**Beryllium BioBank**





# Process Flow



# Eligibility

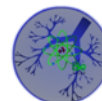
Worked at DOE facility/vendor & potential for beryllium exposure

## Definitive Diagnosis of CBD

- Immune response to beryllium (one)
- abnormal blood BeLPTs
- abnormal BAL BeLPT
- positive skin patch test to beryllium
  - Plus:
- Non-caseating granulomatous lung inflammation (CXR, CT, Pathology Report)

## Probable CBD diagnostic criteria

- Immune response to beryllium, plus one of the following:
- radiologic abnormalities consistent with granulomatous inflammation and sarcoidosis including ground glass infiltrates, centrilobular nodules, or fibrosis.
- OR
- abnormal BAL BeLPT with BAL lymphocytosis.



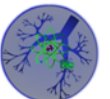
# Eligibility cont.

## BES diagnostic criteria

- Immune response to beryllium (must have evidence of one listed below)
- two positive blood BeLPT
- one positive BAL BeLPT
- positive skin patch test
- Plus:
- absence of pathology consistent with CBD (CXR, CT, Pathology Report)

## BeExposed Controls

- At least one normal BeLPT and no abnormal BeLPT



# Subjects Enrolled

- Individuals with BeS who had initial or follow-up clinical evaluation to determine if CBD;
- Patients with CBD who had follow-up clinical evaluation to determine progression of disease; AND
- Current or former workers: beryllium exposed, involved in medical surveillance to determine sensitization status.



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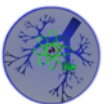


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**Beryllium BioBank**



# Data & Specimen Collection

Written informed consent obtained prior to entry.

- ☐ Questionnaires: Demographic , occupational history /exposure
- ☐ Blood samples: 60 ml; plasma and blood cells, with the option of including DNA extraction

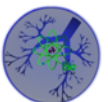
Retrospective data review/retrieval of:

- ☐ existing biopsy specimens
- ☐ clinical data from medical records:
  - ☐ BeLPTs, PFTs, Ex tol, CXR, CT scan
  - ☐ Radiology films
  - ☐ Radiology and pathology reports



Prospective collection:

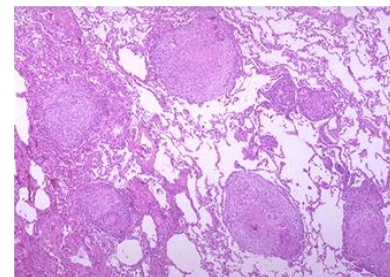
- ☐ clinical data & biological specimens collected at visit
- ☐ Leftover bronchoalveolar lavage fluid, cells and /or biopsy from a clinical bronchoscopy



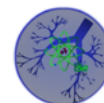
# Data & Specimen Collection

Specimens and data collected at clinical evaluation:

- ☐ **Blood**: A peripheral blood sample of 60 ml; plasma and blood cells, with the option of including DNA extraction
- ☐ **Questionnaire**: an interviewer-administered questionnaire to obtain demographics, medical history, clinical symptoms and occupational and exposure history
- ☐ **Clinical Data**: including permission to review medical evaluation, BeLPT results, physiologic, radiographic and bronchoscopic studies
- ☐ **Other specimens**: BAL fluid and cells, and transbronchial biopsy tissue obtained from clinical evaluation if available

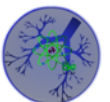
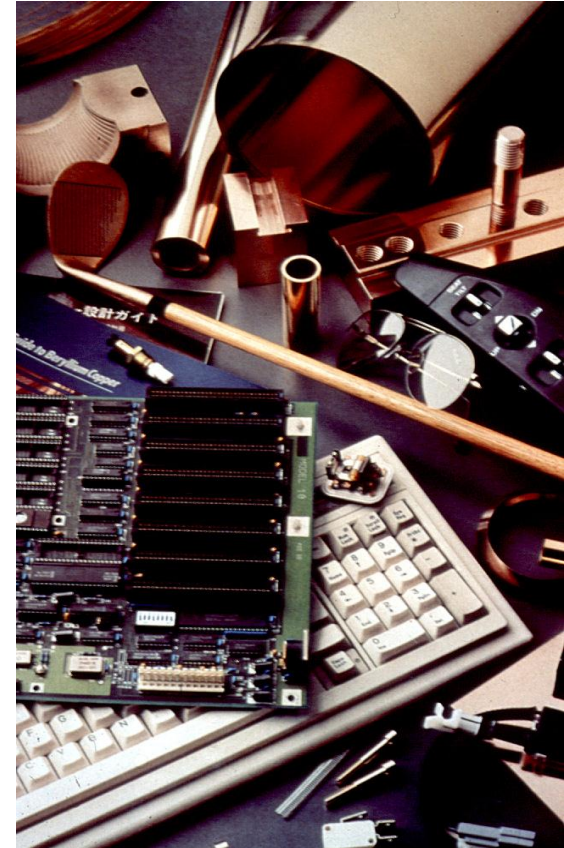


**Beryllium BioBank**



# Questionnaires

- Interviewer-administered
- Demographics
- Medical history
- Clinical symptoms
- Occupational and exposure history
- Obtained on 550 participants

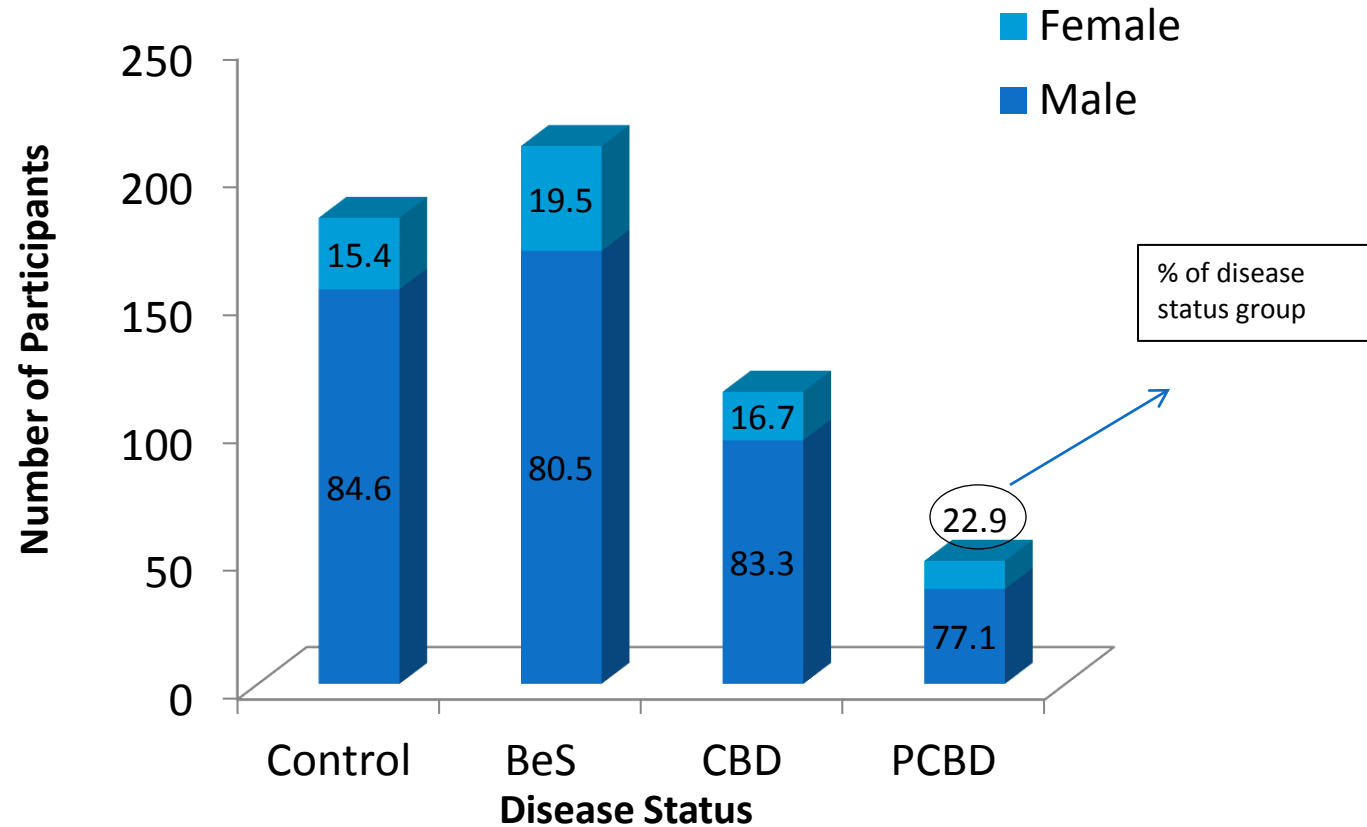


# Participants Enrolled

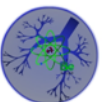
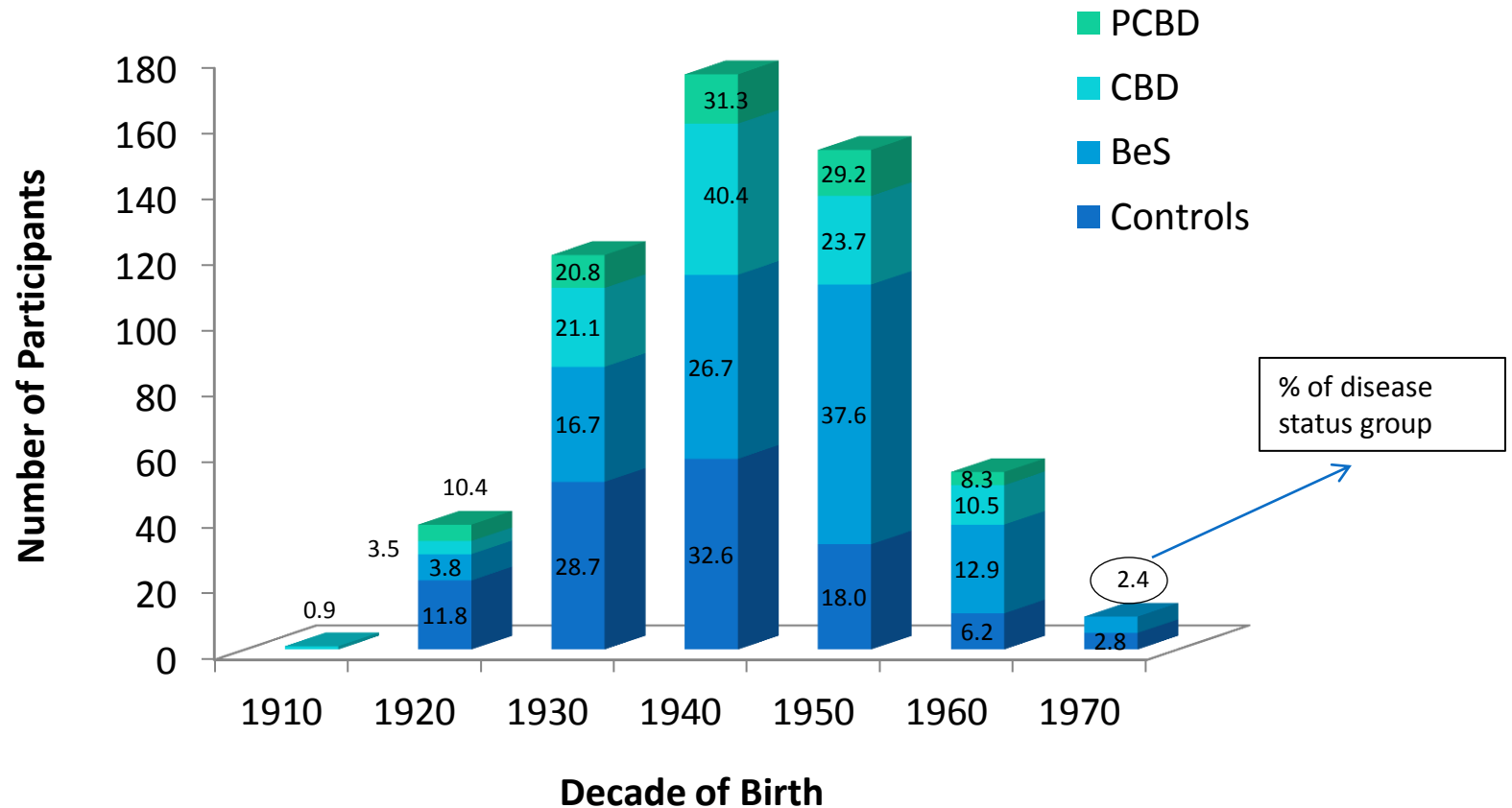


Disease Status	Number Enrolled
Beryllium Exposed Controls (BeNS)	182
Beryllium Sensitized (BeS)	189
Chronic Beryllium Disease (CBD)	109
Probable Chronic Beryllium Disease (PCBD)	48

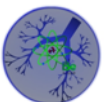
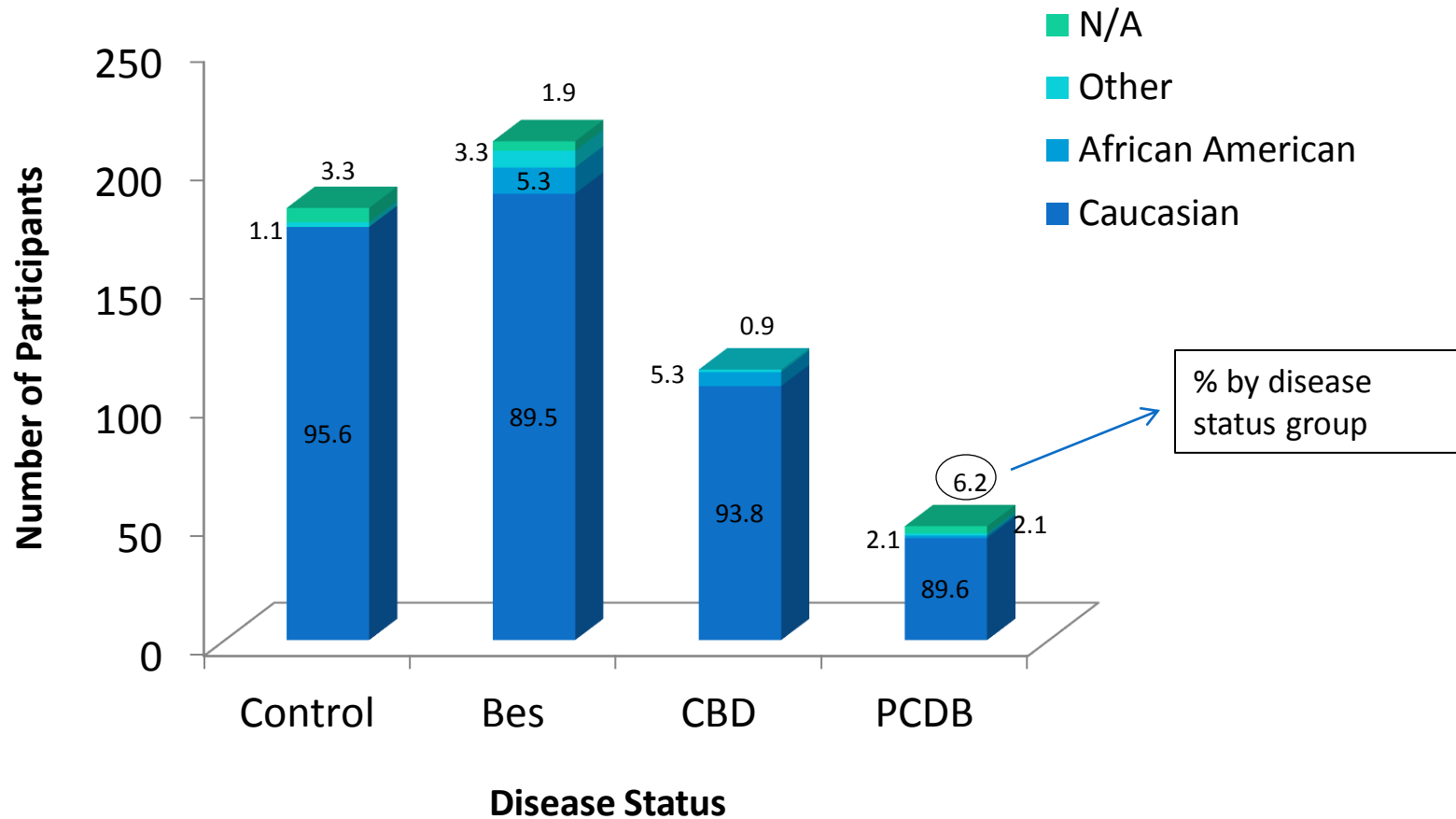
# Demographics: Sex



# Decade of Birth/Age

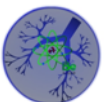


# Demographics: Race



# Available Clinical Data

Data	# Available	# of Participants
PFT	673	345
Pathology Report	374	273
Patch Test	6	5
Blood BeLPT	1377	334
Lavage BeLPT	491	281
Laboratory Reports	513	278
CT Reports/Scans	338	285
CXR Reports	394	253
B-reads	206	153
Exercise Test Data	402	220



PFT				
Baseline visit	BeS	CBD	PCBD	BeNS
FVC (L)	4.09	4.11	4.19	4.59
FEV1 (L)	3.10	3.20	3.21	3.17
DLCO (ml/min/mmHg)	27.32	27.65	25.94	28.76
Baseline visit: Data collected at patient's first clinical evaluation				

PFT		
Progression visit	CBD	PCBD
FVC (L)	3.76	3.84
FEV1 (L)	2.92	2.85
DLCO (ml/min/mmHg)	23.36	25.14
Progression Visit: Data collected at time of progression from BeS to CBD		

Data also available from:

- Start of Treatment: When started on systemic therapy
- Follow-up Visit (s): Visit(s) occurring during the 3 year collection period

# PFT data

- Data is for all PFT tests and laboratory tests, not individuals
- Missing data, e.g. DLCO
  - BeNS: 87/180 (48.3%)
  - BeS-144/276 (52.2%)
  - CBD- 73/152 (48.0%)
  - PCBD 27/56 (48.2%)



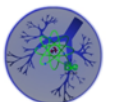
# Other data

## % Lymphocyte from BAL

Baseline visit	BeS	CBD	PCBD	BeNS
% BAL Lymph	9.46	18.75	18.97	N/A
Baseline visit: Data collected at patient's first clinical evaluation				

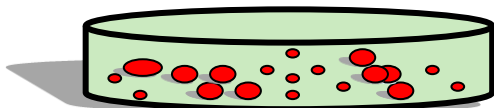


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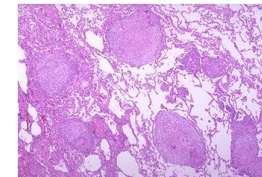
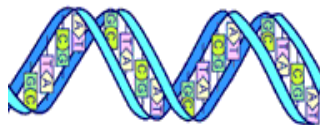


# Available Blood & Other Specimens

Specimen Collection Type	Total Specimens Available	Total CBD (including PCBD) Specimens	Total BeS Specimens	Total Control Specimens
Blood: PBMC	487	145	177	101
Blood : DNA	511	151	183	177
Blood: Plasma	502	147	147	172
BALF/ cells	85	24	62	NA
Transbronchial biopsy tissue	216	72	142	2



**Blood cells**



# Archival Storage Conditions

Specimen Type	Condition
Paraffin blocks	Room temperature
Slides	-20°C or -80°C
Blood-plasma	-80°C
BALF	-80°C
Blood cell pellet	Liquid nitrogen
BAL cell pellet	Liquid nitrogen
DNA	-80°C



Request by Investigators for  
Specimens/Data  
(via DCC)

Review Committee Process

Request accepted

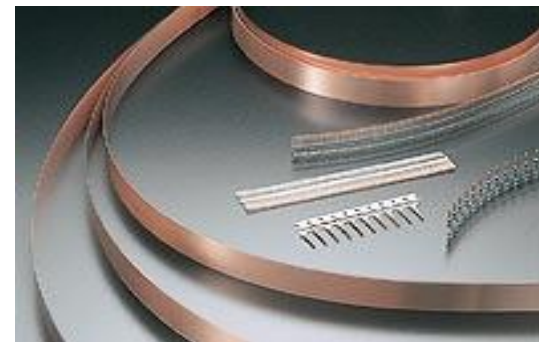
UCD contacts  
researcher to review  
request

Specimen release  
request sent from  
UCD to NJH

NJH ships specimens to  
researcher

Data Mining  
(UCD)

Data sent to  
researcher (UCD)



# Application Process

# Application for Data and Sample Use

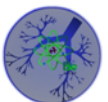
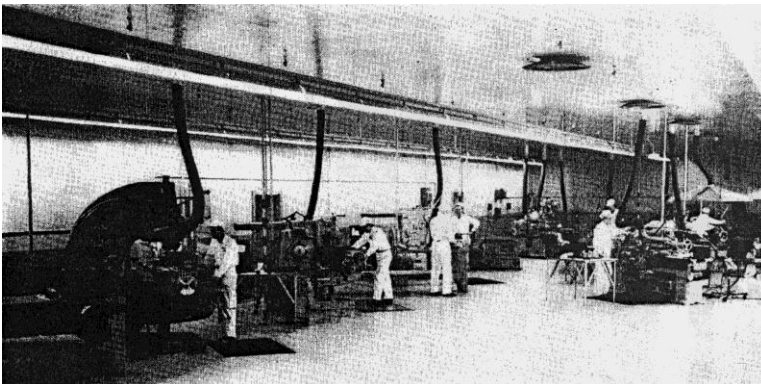
- **Abstract**
- **Prior Research-** importance of the proposed research topic
- **Major Goals of the Research-** specific hypotheses
- **Subjects-** inclusion/exclusion criteria, comparison groups, etc.
- **Analysis Variables-** outcome dependent variables, independent variables, other variables to consider in analysis.
- **Statistical Methods/Approaches-** anticipate using, Power/Justification for the number of specimens required.
- **Feasibility-** Timeline, methods already established?

## **Additional Application Requirements**

- Specimen Request Form: patient groups and data/specimens requested
- Investigator and Institutional Certification Document
- Biographical sketch

# Research Review Committee

- PI's from each Clinical Center and DCC
- DOE Representative
- Steering Committee Chair
- Invited participants:
  - 3 year commitment
  - Quarterly teleconference
  - Review proposals
  - Recommendations for specimen use



# Review of Applications: NIH Review

## Scientific Merit

- Does the research address an important problem in beryllium research?
- If the study aims are to be achieved, how will scientific knowledge be advanced?
- Does the study involve novel concepts, approaches and methods?

## Approach

- Are the conceptual framework, design, methods and statistical analyses adequately developed, well intergraded, and appropriate to the aims of the project?

## Feasibility

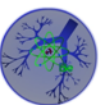
- Can the project be accomplished in the timeline presented?
- Are the expertise available suitable for the proposed study?

## Sample Use

- Best use of the available samples?

## Funding/Staff

- Is the funding in place for this project?
- Are staff currently in place for this project?



# Contact Information

**NJH** PI: Lisa Maier, MD, MSPH

[MaierL@NJHealth.org](mailto:MaierL@NJHealth.org)

Coordinator: Briana Barkes, MPH

[BarkesB@NJHealth.org](mailto:BarkesB@NJHealth.org)

**DCC** PI: Lee Newman, MD, MA

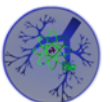
[Lee.Newman@ucdenver.edu](mailto:Lee.Newman@ucdenver.edu)

Coordinator: Kaylan Stinson, MSPH

[Kaylan.Stinson@ucdenver.edu](mailto:Kaylan.Stinson@ucdenver.edu)

<http://www.ucdenver.edu/berylliumbiobank>

**Beryllium BioBank**



# Project Investigators & Research Team

## **Clinical Centers:**

### **University of Pennsylvania**

- Milt Rossman, MD
- Barbara Finkel, MSN, RN
- Leota Terry

### **University of California, San Francisco**

- John Balmes, MD
- Mary DeJesus
- Judie Guerriero

### **University of California, Los Angeles**

- Philip Harber, MD
- Samantha Wu

### **East Tennessee Pulmonary Associates**

- Charles Bruton, MD\*
- Pamela Pigg, RN

### **Oak Ridge Associated Universities**

- Donna Cragle, PhD

## **Lead Clinical Center:**

### **National Jewish Health**

- Lisa Maier, MD, MSPH
- Briana Barkes, MPH
- Christina Gastiopoulos
- May Gillespie
- Jill Elliott
- Gina Mondello

## **Data Coordinating Center:**

### **University of Colorado, CSPH**

- Lee Newman, MD, MA
- Kaylan Stinson, MSPH
- Ray Kasel

## **Department of Energy**

- Bonnie Richter, PhD
- Marsha Lawn\*
- Clifton Strader, PhD

